Claims 1 and 16 have been amended to more clearly define the claimed subject matter. The specification has been amended to correct obvious typographical errors. New claims 19-20 are added. Support for claims 19 and 20 is found in the present specification at page 4, line 22. Accordingly, the amendments do not constitute the addition of new matter. Applicant respectfully requests the entry of the amendments and reconsideration of the application in view of the amendments and the following remarks. Claims 1-20 are now pending in this application.

The specific changes to the specification and the amended claims are shown on a separate set of pages attached hereto and entitled **VERSION WITH MARKINGS TO SHOW CHANGES MADE**, which follows the signature page of this Amendment. On this set of pages, insertions are underlined and deletions are struck through.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 1, 16 and claims dependent thereon are rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claims 1 and 16 have been amended as suggested by the Examiner. In view of Applicants' amendments, reconsideration and withdrawal of this ground of rejection is respectfully requested.

Rejections under 35 U.S.C. § 103(a)

Claims 1-5, 8, 11, and 13-18 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ikada et al. (U.S. Patent 4,743,258).

The Examiner asserts that Ikada et al. teach that polymers may be attached to the surface of a substrate material by graft polymerizing monomers to the surface via peroxide radicals formed in low temperature plasma discharge. While Ikada et al. fail to teach the source of the peroxide radicals, the Examiner further asserts that it would have been obvious to one of ordinary skill in the art to select hydrogen peroxide from the class of peroxides taught by Ikada.

In response, Ikada et al. do not teach or suggest sterilization by any means. There is no teaching in Ikada et al. that plasma provided for surface modification would provide adequate sterilization and one of ordinary skill in the art would not have assumed that the graft polymerization process of Ikada et al. would inherently result in sterilization as asserted by the Examiner.

Not all plasma can act as a sterilizer. For example, Table I of U.S. Patent 4,643,876 (Exhibit A) illustrates that H_2O_2/plasma performs much better than other gas/plasma systems when all tests were performed under the same reaction conditions. Consequently, one of ordinary skill in the art would not assume that the peroxide radicals produced in the practice of the method disclosed in Ikada, et al. would provide for sterilization in the absence of a specific teaching.

Furthermore, under the specific conditions of the '876 patent (Exhibit A), the efficacy of H_2O_2 with regards to sterilization is concentration dependent as shown in Table 2 of the '876 patent (Exhibit A). Concentrations of H_2O_2 of 0.208 mg/ liter or less were not adequate to provide complete sterilization under the conditions of the '876 patent. There is no teaching in Ikada et al. on the peroxide level achieved by the practice of their described method and it cannot be assumed that the level of peroxide produced by the method of Ikada et al. was sufficient to provide sterilization. Consequently, the process of Ikada, et al. would not inherently result in sterilization as one of ordinary skill in the art could not predict, based upon the Ikada et al. disclosure, that sterilization would necessarily follow from the practice of the claimed method.

It is further noted that the irradiation times in Ikada, et al. are either not provided or they are very short. Example 1 is silent with respect to time. In Example 2, the corona discharge is only conducted for 30 seconds (col. 5, line 20) and in Example 3 the argon gas plasma is conducted for 30 seconds (col. 5, line 43). It is respectfully submitted that these time periods are not long enough to allow for sterilization at the stipulated energy levels.

Furthermore, the order of the steps and the plasma power are important. As shown in Example V and Table V of '876 (Exhibit A), under the given test conditions, if the peroxide is introduced while the plasma is generated, sporicidal activity is only observed with lower power levels. At higher power levels, the hydrogen peroxide dissociates before it can diffuse to the sample so very poor sporicidal activity is observed (col. 8, lines 48-53). In Example 1 of Ikada et al., the sample is gamma irradiated, then desiccated, and then dipped in an aqueous solution containing acrylamide (see col. 4, lines 35-45). As argued above, there is no assurance that the practice of the method of Ikada et al. would have produced any sterilization at all. Furthermore, as indicated by the evidence of Exhibit A, the procedure of Ikada et al. would have produced, at best, incomplete and inefficient sterilization due to introduction of the plasma before the peroxide had diffused sufficiently into the material. Even if sterilization does occur in the

described method(s) of Ikada et al., it is not evident from a plain reading of the specification that sterilization would be maintained through the subsequent steps such as desiccation and dipping into the acrylamide solution. In contrast, in Applicants' claimed method, sterilization is always the last step (see Figure 1 of the present application).

In summary, sterilization is neither taught nor suggested by the cited reference. Furthermore, it would not have been apparent to one of ordinary skill in the art at the time of the claimed invention that sterilization would inherently occur under the conditions set forth by Ikada, et al. as discussed above. Additionally, there is no assurance that whatever sterilization may inherently occur would be compatible with the coating material and there is no assurance that sterilization would be maintained throughout the subsequent coating steps. Consequently, Ikada et al. cannot render obvious Applicants' claimed invention.

In view of Applicants' arguments, reconsideration and withdrawal of this ground of rejection is respectfully requested.

Claims 1-5, 8, and 16-18 are rejected under 35 U.S.C. § 103(a) as unpatentable over Akagi et al.

Akagi et al are cited for teaching polymerization of monomers by a peroxide process. Again the Examiner asserts that the graft polymerization process of Akagi would have inherently resulted in sterilization of the substrate material.

This ground of rejection is similar to the rejection over Ikada et al. discussed above and the arguments presented for the rejection over Ikada et al. are incorporated herein by reference.

Akagi et al. are concerned with a coating for polyester fabric which prevents dye migration and sublimation (col. 6, lines 50-54, for example). Akagi et al. do not teach or suggest sterilization. Akagi et al. teach the use of O_2 has to form a low temperature plasma (col. 9, lines 53-66). As seen from Table I of U.S. Patent 4,643,876 (Exhibit A) O_2/plasma had very little sporicidal activity under the conditions used. Thus, there is reason to believe that sterilization would not necessarily occur under the conditions taught by Akagi. Consequently, sterilization is not inherent to the method of Akagi et al.

Furthermore, it cannot be assumed that the peroxide species generated by the process of Akagi, et al. would be sufficient to provide sterilization because it is not clear if the peroxide species are present at a sufficient concentration. As evidenced by Table II of Exhibit A discussed above in the response to the rejection over Ikada et al., lower concentrations of peroxide were not

effective to provide sterilization under the conditions tested. Consequently, the process of Akagi et al. would not have inherently resulted in sterilization because one of ordinary skill in the art would not predict that sterilization would necessarily follow from the practice of the method of Akagi et al.

In view of the arguments presented above, reconsideration and withdrawal of this ground of rejection is respectfully requested.

Claims 1, 3, and 5-15 are rejected under 35 U.S.C. § 103(a) as unpatentable over Hendriks in view of Spencer.

The Examiner asserts that Hendriks teaches graft polymerizing polymers and sterilization by ethylene oxide. Spencer is cited for his teaching on the use of hydrogen peroxide sterilization. The Examiner asserts that Spencer reasonably suggests the use of hydrogen peroxide sterilization as an alternative to the ethylene oxide method taught by Hendriks.

In response, there is no motivation to combine the teaching of Spencer with the teaching of Hendriks. There is no teaching in either reference that would lead one of ordinary skill in the art to substitute the sterilization method of Spencer for the sterilization method of Hendriks. As taught by the present specification, the stability of the bioactive coating is negatively impacted by conventional sterilization methods (see present specification at page 4, lines 13-14). Indeed, the use of gamma sterilization and e-beam sterilization (present specification, Table 2 at page 13) and argon plasma (present specification, Table 3 at page 14) resulted in lower PEG incorporation and heparin grafting compared to the claimed process.

In order to provide a prima facie case of obviousness, the Patent and Trademark Office has the burden to provide a motivation, teaching or suggestion to create the claimed invention. *See, e.g., In re Fine*, 5 U.S.P.Q.2d 1597 (Fed. Cir. 1988). Such motivation, teaching or suggestion is absent in the references cited by the Examiner. As indicated by the present specification, especially Tables 2 and 3 of the present specification, one of ordinary skill in the art would not merely combine a coating method with a sterilization method with a reasonable expectation of success because, as indicated by the specification, several commonly used sterilization methods have deleterious effects upon the bioactive coating. It is not predictable, based upon the cited references, that the method of polymerizing a bioactive coating onto a material as taught by Hendriks et al. could be combined with the process of Spencer et al. with a reasonable expectation of success.

Further, as the Federal Circuit observed in *Orthopedic Equipment Co. v. United States*, 702 F.2d 1005, 217 U.S.P.Q. 193 (Fed. Cir. 1983), it is "wrong to use the patent in suit as a guide through the references in the right way so as to achieve the result of the claims in suit". The use of hindsight is not permissible in combining references to formulate a rejection under 35 U.S.C. § 103. The motivation to combine the references must come from the references themselves and not from Applicants' teaching.

In view of Applicants' arguments, reconsideration and withdrawal of this ground of rejection is respectfully requested.

CONCLUSION

In view of Applicants' amendments to the claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: July 1, 2002

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Table 2 on page 13 of the specification has been amended as follows:

Table 2: Comparison to other sterilization methods

Exposure Technique	% Atoms on Surface Detected by XPS after PBS challenge	
	O/C* ~~(s.d.)~~	S^ ~~(s.d.)~~
Gamma sterilization (5 Mrad)	0.1	0.04
e-beam sterilization (5 Mrad)	0.13	0.04
STERRAD Sterilization grafted (500W)	0.40	**0.26**
XPS data are generally reported to one significant digit beyond the decimal point. For the early data, results were reported to one significant digit. The later data were reported to two significant digits so that 0.24 and 0.26 are not thought to differ by a factor of 1.5, i.e. 0.2 vs. 0.3.		

*O/C numbers higher than the control are indicative of a PEG group on the surface (PEG having more oxygen than PU); detection of coating on surface.

^S is indicative of heparin on the surface.

IN THE CLAIMS:

Claims 1 and 16 have been amended as follows:

Claim 1. (Amended) A method of sterilizing a material comprising:

applying ~~said material with~~ a bioactive coating comprising polymerizable chemical to said material;

polymerizing said bioactive coating on said material; and

sterilizing said material and said bioactive coating with a sterilization process comprising generating a hydrogen peroxide ~~employing~~ gas plasma.

Claim 16. (Amended) A method of sterilizing and polymerizing a bioactive coating on a material comprising:

applying ~~said material with~~ a bioactive coating comprising non-polymerized but polymerizable chemical to said material; and

simultaneously polymerizing said bioactive coating and sterilizing said material and bioactive coating with a sterilization process comprising generating a hydrogen peroxide ~~employing~~ gas plasma.

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EXHIBIT A